JC17 Rec'd PCT/PTO 0 7 DEC 2001

# TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER WPT0006

U.S. APPLICATION NO (IF KNOWN)

10/ 009277											
INTE		ONAL APPLICATION NO. CT/GB00/02259	INTERNATIONAL FILING DATE 9 June 2000	PRIORITY DATE CLAIMED 9 June 1999							
TITLE OF INVENTION MIXING APPARATUS AND METHOD OF MIXING DURING CONDUCTING AN ASSAY											
APPLICANT(S) FOR DO/EO/US David ANDREWES, et al.											
Applicant herewith submits to the U.S. Designated/Elected Office (DO/EO/US) the following items and other information:											
1.	$\boxtimes$	This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.									
2.		This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.									
3.		This is an express request to begin national examination procedures (35 U.S.C. 371(f) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).									
4.	$\boxtimes$	A proper Demand for International Preliminary Examination was made by the 19 <sup>th</sup> month from the earliest claimed priority date.									
5.	$\boxtimes$	A copy of the International Application as filed (35 U.S.C. 371(c)(2)).									
		a.  is transmitted herewith (required only if not transmitted by the International Bureau)									
		b. As been transmitted by the International Bureau.									
6.	П	c. is not required, as the application was filed in the United States Receiving Office (RO/US).  A translation of the International Application into English (35 U.S.C. 371(c)(2)).									
7.											
,	ر د	Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).  a.  are transmitted herewith (required only if not transmitted by the International Bureau).									
		b.  have been transmitted by the International Bureau.									
	•		nade; however, the time limit for making nade and will not be made.	such amendments has NOT expired.							
8.		A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).									
9.	$\boxtimes$	An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)) (unsigned).									
10.		A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).									
Items	s 11 to	16 below concern documen	t(s) or information included:								
11.	×	PCT Search Report and International Preliminary Examination Report.									
12.		An assignment document for recording. A separate cover sheet is included.									
13.	$\boxtimes$	A FIRST preliminary amendment.									
14.		A substitute specification.									
15.		A change of power or attorney and/or address letter.									
16.	$\boxtimes$	Other items or information									
		Certificate of Mailing by Express Mail and Return Card; IDS, Form 1449 and copies of references; Check for \$1,704.00.									

$egin{array}{cccc} {}^{ m APPLICATION NO. (lf kr)} & 10 & 00 \end{array}$	277 AF	APPLICATION NO. (If known)			WPT0006						
17. 🛛 The following	ng fees are submit	bmitted (Applicant is small entity)			CALCULATIONS						
BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)  Search Report has been prepared by the EPO or JPO											
Surcharge of <b>\$130.0</b> 30 ⊠ months from t	\$ 130.00										
CLAIMS	NUMBER FIL	.ED		RATE							
Total Claims	31 - 20 =	11	1	x \$ 18.00	\$198.00						
Independent Claims	7 - 3 =	4		x\$ 84.00	\$336.00						
				+ \$280.00	\$0						
	\$1,704.00										
Reduction by ½ for filing by must also be filed (Note 37	\$.00										
	\$0										
Processing fee of \$130.00 months from the earliest cl	\$0										
	\$0										
Fee for recording the encloaccompanied by an approp	+ \$0										
		TOTA	L NATION	AL FEE =	\$1,704.00						
					Amount to be: refunded	\$					
					charged	\$					
<ul> <li>a.  \( \subseteq \) A check in the amount of \$1,704.00 to cover the above fees is enclosed.</li> <li>b.  \( \subseteq \) Please charge my Deposit Account No in the amount of \$ to cover the above fees.</li> <li>c.  \( \subseteq \) The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-1123.</li> <li>NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b) must be filed and granted to restore the application to pending status.</li> </ul>											
or (b) must be filed and granted to restore the application to perform status.  SEND ALL CORRESPONDENCE TO:											
Carol W. BURTON, Esq. Hogan & Hartson, L.L.P. One Tabor Center Suite 1500 1200 Seventeenth Street Denver, Colorado 80202  Reg. No. 42,320											

Attorney Docket No. WPT0006 Client Matter No. 80469.0006

# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE UNDER THE PATENT COOPERATION TREATY

In re Application of:

David ANDREWES, et al.

Serial No. Unassigned

Filed: December 7, 2001

For: APPARATUS, INSTRUMENT AND

**DEVICE FOR CONDUCTING AN ASSAY** 

Examiner: Unassigned

Art Unit: Unassigned

#### PRELIMINARY AMENDMENT

Assistant Commissioner for Patents 2900 Crystal Drive Arlington, VA 22202-3513

Sir:

Please amend the copy of PCT Patent Publication No. WO 00/76642 A2, filed herewith, as follows:

#### IN THE CLAIMS

Please cancel claims 32–35 without prejudice to the subject matter contained therein.

Please amend the claims 1–31 according to the attached sheets.

#### REMARKS

The amendment cancels claims 32–35, making claims 1–31 pending in the application. The amendment removes the multiple dependent claim format and reference numbers in the claims, and is not made to overcome any prior art references. Support for the amendment can be found in the claims. No new matter has been added by the amendment.

Please consider the pending claims in light of the references cited in the enclosed Information Disclosure Statement. These references were cited in the PCT International Search Report, a copy of which is enclosed for your convenience. Applicants enclose herewith the fee for filing a continuation application and believe this to be the only fee required for this amendment and response. Should any additional fees be required, please charge Deposit Account 50-1123.

Respectfully submitted,

December 7, 2001

Eugené J. Bernard, Reg. No. 42,320

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# MARKED-UP VERSION OF THE CLAIMS

- 1. A method of mixing a sample in a chamber [(3, 5)] comprising the steps of positioning a paddle [(100)] in the sample and causing said paddle to undergo a reciprocating motion.
- 2. A method a claimed in claim 1 wherein the paddle is of a magnetic material and comprises a liquid moving surface and means for supporting the paddle in or over the chamber and said paddle is caused to undergo a reciprocating motion by the action of an electromagnetic means.
- 3. A method as claimed in claim 2 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface which arms sit in a pair of slots in sides extending from a base which defines the chamber.
- 4. A method as claimed in [either] claim 2 [or 3] which [further] comprises the steps of detecting an analyte in said sample by passing a light beam from a light emitter through said chamber and an opening [(106)] formed in the liquid moving surface of said paddle to a light detector.
- 5. A method as claimed in claim 4 wherein the sample is glycated haemoglobin and is detected by a spectrophotometric means at between 405 nm and 460 nm.
- 6. A paddle [(100)] comprising a liquid moving surface and means for supporting said paddle in or over a chamber such that the paddle can undergo a reciprocating motion in the chamber.
- 7. A paddle as claimed in claim 6 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface.
- 8. A paddle as claimed in [either] claim 6 [or 7] wherein the paddle is T shaped.

- 9. A paddle as claimed in [any of] claim 6[,7 or 8] wherein the liquid moving surface has an opening [(106)] formed therein through which a light beam can pass.
- 10. A paddle as claimed in [any of] claim[s] 6 [to 9] wherein the paddle comprises a magnetic material.
- 11. A paddle as claimed in [any of] claim[s] 6 [to 9] wherein the paddle comprises a piezoelectric material.
- 12. A sample container comprising <u>a</u> chamber [(3, 5)] adapted to receive a paddle [(100)], said paddle being mounted in or over said chamber such that the paddle can undergo a reciprocating motion in the chamber.
- 13. A sample container as claimed in claim 12 comprising a base with sides extending therefrom to define the chamber, said sides comprising means which support the paddle.
- 14. A sample container as claimed in claim 13 wherein said means which support the paddle is a pair of slots in said sides.
- 15. A sample container as claimed in [any of] claim[s] 12[-14] in which said chamber is an optical chamber.
- 16. A sample container as claimed in [any of] claim[s] 12[-15] which is a carousel or cassette.
- 17. A [carousel] <u>sample container</u> as claimed in claim 16, <u>which is a carousel</u> for use in an assay in which a sample is separated into a first component fraction and a second component fraction, which fractions are presented to an instrument, comprising a first inlet which is or leads to a first component fraction collection chamber, a second inlet which is or leads to a second component fraction collection chamber, and an inlet port accommodating a filter means or a binder retaining means, said inlet port being movable relative to each of said first and second inlets such that the inlet port can be brought into liquid communication with each first and second inlet in turn as required.

- 18. A sample container as claimed in claim 16 which is a carousel comprising a base portion having a plurality of chambers including first and second inlets, a top portion which together with the base portion forms the carousel, and a funnel portion including an inlet port, said carousel being rotatably mounted about said funnel portion.
- 19. An [instrument] <u>apparatus</u> adapted to receive a sample container comprising a chamber adapted to receive a paddle, said instrument comprising means for causing said paddle to undergo a reciprocating motion in the chamber.
- 20. An apparatus as claimed in claim 19 in which said means for causing said paddle to undergo a reciprocating motion is an electromagnetic means.
- 21. An apparatus as claimed in claim 20 wherein said electromagnetic means is a solenoid.
- 22. A device comprising an instrument capable of detecting an analyte in a sample which is presented thereto in a sample container comprising a chamber adapted to receive a paddle said paddle being mounted in or over said chamber such that said paddle can undergo a reciprocating motion when initiated by said instrument.
- 23. A device, comprising an instrument for reading one or more samples, and an apparatus for presenting the one or more samples to the instrument, wherein the positioning of the one or more samples into a reading position is achieved using two phased recognition.
- 24. A device as claimed in claim 23 in which a first switch informs the instrument that the apparatus is within range and a second switches confirms precise alignment.
- 25. A device as claimed in claim 23 [or 24] wherein a first micro switch on the instrument is activated by an ["]element["] on the apparatus and this constitutes the first phase of detection and a second switch on the

instrument serves as [the]  $\underline{a}$  ["]fine tune["] and is activated when the instrument reaches a precise location on the instrument.

- 26. A device as claimed in claim 25 wherein the ["]element["] on the apparatus is a projecting member which depresses a board mounted microswitch via a rocker arm assembly.
- 27. A device as claimed in claim 26 wherein the two members of the switch are a notch in the outermost wall of the apparatus, and a resilient member or arm on the instrument.
- 28. A device as claimed in claim 27 wherein the apparatus is a carousel or cassette type apparatus.
- 29. A device as claimed in claim 28 comprising four switches located 90° apart.
- 30. A method for determining the percentage glycation of blood comprising the steps of separating a blood sample into a first component fraction containing one or more non glycated proteins, and a second component containing the one or more glycated protein and detecting/quantifying glycated haemoglobin by spectrophotometric means at between 405 nm and 460 nm.
- 31. A method as claimed in claim 30 wherein the detection/quantification of glycated haemoglobin is measured at about 440 nm.

### **CLEAN VERSION OF THE CLAIMS**

- A method of mixing a sample in a chamber comprising the steps of positioning a paddle in the sample and causing said paddle to undergo a reciprocating motion.
- 2. A method a claimed in claim 1 wherein the paddle is of a magnetic material and comprises a liquid moving surface and means for supporting the paddle in or over the chamber and said paddle is caused to undergo a reciprocating motion by the action of an electromagnetic means.
- 3. A method as claimed in claim 2 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface which arms sit in a pair of slots in sides extending from a base which defines the chamber.
- 4. A method as claimed in claim 2 which comprises the steps of detecting an analyte in said sample by passing a light beam from a light emitter through said chamber and an opening formed in the liquid moving surface of said paddle to a light detector.
- 5. A method as claimed in claim 4 wherein the sample is glycated haemoglobin and is detected by a spectrophotometric means at between 405 nm and 460 nm.
- 6. A paddle comprising a liquid moving surface and means for supporting said paddle in or over a chamber such that the paddle can undergo a reciprocating motion in the chamber.
- 7. A paddle as claimed in claim 6 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface.
  - 8. A paddle as claimed in claim 6 wherein the paddle is T shaped.
- 9. A paddle as claimed in claim 6 wherein the liquid moving surface has an opening formed therein through which a light beam can pass.

- 10. A paddle as claimed in claim 6 wherein the paddle comprises a magnetic material.
- 11. A paddle as claimed in claim 6 wherein the paddle comprises a piezoelectric material.
- 12. A sample container comprising a chamber adapted to receive a paddle, said paddle being mounted in or over said chamber such that the paddle can undergo a reciprocating motion in the chamber.
- 13. A sample container as claimed in claim 12 comprising a base with sides extending therefrom to define the chamber, said sides comprising means which support the paddle.
- 14. A sample container as claimed in claim 13 wherein said means which support the paddle is a pair of slots in said sides.
- 15. A sample container as claimed in claim 12 in which said chamber is an optical chamber.
- 16. A sample container as claimed in claim 12 which is a carousel or cassette.
- 17. A sample container as claimed in claim 16, which is a carousel for use in an assay in which a sample is separated into a first component fraction and a second component fraction, which fractions are presented to an instrument, comprising a first inlet which is or leads to a first component fraction collection chamber, a second inlet which is or leads to a second component fraction collection chamber, and an inlet port accommodating a filter means or a binder retaining means, said inlet port being movable relative to each of said first and second inlets such that the inlet port can be brought into liquid communication with each first and second inlet in turn as required.
- 18. A sample container as claimed in claim 16 which is a carousel comprising a base portion having a plurality of chambers including first and second inlets, a top portion which together with the base portion forms the carousel, and a funnel portion including an inlet port, said carousel being rotatably mounted about said funnel portion.

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- 19. An apparatus adapted to receive a sample container comprising a chamber adapted to receive a paddle, said instrument comprising means for causing said paddle to undergo a reciprocating motion in the chamber,
- 20. An apparatus as claimed in claim 19 in which said means for causing said paddle to undergo a reciprocating motion is an electromagnetic means.
- 21. An apparatus as claimed in claim 20 wherein said electromagnetic means is a solenoid.
- 22. A device comprising an instrument capable of detecting an analyte in a sample which is presented thereto in a sample container comprising a chamber adapted to receive a paddle said paddle being mounted in or over said chamber such that said paddle can undergo a reciprocating motion when initiated by said instrument.
- 23. A device, comprising an instrument for reading one or more samples, and an apparatus for presenting the one or more samples to the instrument, wherein the positioning of the one or more samples into a reading position is achieved using two phased recognition.
- 24. A device as claimed in claim 23 in which a first switch informs the instrument that the apparatus is within range and a second switches confirms precise alignment.
- 25. A device as claimed in claim 23 wherein a first micro switch on the instrument is activated by an element on the apparatus and this constitutes the first phase of detection and a second switch on the instrument serves as a fine tune and is activated when the instrument reaches a precise location on the instrument.
- 26. A device as claimed in claim 25 wherein the element on the apparatus is a projecting member which depresses a board mounted microswitch via a rocker arm assembly.

- 27. A device as claimed in claim 26 wherein the two members of the switch are a notch in the outermost wall of the apparatus, and a resilient member or arm on the instrument.
- 28. A device as claimed in claim 27 wherein the apparatus is a carousel or cassette type apparatus.
- 29. A device as claimed in claim 28 comprising four switches located 900 apart.
- 30. A method for determining the percentage glycation of blood comprising the steps of separating a blood sample into a first component fraction containing one or more non glycated proteins, and a second component containing the one or more glycated protein and detecting/quantifying glycated haemoglobin by spectrophotometric means at between 405 nm and 460 nm.
- 31. A method as claimed in claim 30 wherein the detection/quantification of glycated haemoglobin is measured at about 440 nm.

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## **DESCRIPTION**

# MIXING APPARATUS AND METHOD OF MIXING

The present invention relates to an improved mixing apparatus and a method of mixing.

More particularly it relates to an improved apparatus, instrument and device for conducting an assay and the assay methodology.

In a particularly preferred embodiment it relates to a device suitable for use in assaying analyses, for example glaciated proteins, in samples such as, for example, blood.

A person skilled in the art will however appreciate that the principle behind the invention can be applied to solve a mixing problem in a number of different apparatus, instruments or devices.

The applicant has developed an apparatus, instrument and device for conducting an assay as disclosed in PCT/GB98/03586. The apparatus comprises a first inlet, a second inlet, and an inlet port, the inlet port being moveable relative to each of said first and second inlets such that the port can be brought into liquid communication with each inlet in turn as required, the inlet port accommodating a filter means and/or a binder retaining means.

In the course of conducting an assay to, for example, determine the presence or absence of one or more analyses in a sample, the sample is separated into a first component fraction and a second component fraction,

the second component fraction being obtained by eluting a component "held".

on the binder retaining means from the binder retaining means.

The applicant has determined that the elution step in which the elutant fills the second inlet under gravity, gives a non-homogenous sample (due to the formation of an elution gradient in the second inlet) which results in inaccurate readings when the sample is "read" in a measuring instrument, such as, for example, an instrument comprising a microprocessor operable via a keypad, one or more light emitters and one or more light detectors, a display and driver, an analogue to digital convertor and means for connecting the instrument to a power source.

It is an aim of the present invention to provide a simple method for making a gravity fed fraction homogenous and more particularly to provide a modified apparatus, instrument and/or device capable of performing such a method.

In accordance with a first aspect of the present invention there is provided a method of mixing a sample in a chamber comprising positioning a paddle in the sample and causing said paddle to undergo a reciprocating motion.

It is another and independent aim of the present invention to provide an apparatus, instrument or device, capable of mixing a sample for an assay in which an analyte is detected by a spectrophotometric means and/or a component for use in achieving this aim. According to a further aspect of the present invention there is provided, a paddle comprising a liquid moving surface and means for supporting said paddle in or over a chamber such that the paddle can undergo a reciprocating motion in the chamber.

Preferably the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface.

Preferably the paddle is T shaped.

More preferably the fluid moving surface has an opening formed therein through which a light beam can pass.

In one embodiment, the paddle comprises a magnetic material and is caused to undergo a reciprocating motion by an electromagnetic means such as a solenoid.

Of course other mechanisms could be used to effect a reciprocating motion. For example, the paddle could comprise a piezoelectric material and be caused to undergo a reciprocating motion using a localised current.

According to yet a further aspect of the present invention there is provided a sample container adapted to receive a paddle said paddle being mounted in or over said sample container such that the paddle can undergo a reciprocating motion in the container.

Preferably the sample container comprises a base with sides extending therefrom to define a chamber, said sides comprising means, for example a pair of slots, which support the paddle.

Preferably the sample container is an apparatus comprising an optical chamber.

More preferably the sample container is part of a carousel or cassette.

According to yet a still further aspect of the present invention there is provided an instrument adapted to receive a sample container comprising a paddle, said instrument comprising means for causing said paddle to undergo a reciprocating motion in the container.

Preferably said means for causing said paddle to undergo a reciprocating motion is an electromagnetic means, for example a solenoid.

According to yet a still further aspect of the present invention there is provided a device comprising a reading instrument comprising means for driving a paddle in a reciprocating manner in an apparatus comprising an optical chamber.

An example of an apparatus and instrument which can be adapted in accordance with the present invention are described in International application PCT/GB98/03586.

The apparatus and instrument described in PCT/GB98/03586 are susceptible to a number of other problems common to devices which are used in assays. Thus, a separate and unrelated problem with a device of the general type described in PCT/GB98/03586, namely one in which a sample or samples are presented to an instrument for reading, is one of accurately positioning the sample relative to, for example, one or more of the light

emitters and one or more light detectors which make up the reading means if reading errors are to be avoided or at least minimized.

Thus it is an independent aim of the present invention to provide a device which enables accurate readings to be taken.

According to this independent aspect of the present invention there is provided a device, comprising an instrument for reading one or more samples, and an apparatus for presenting the one or more samples to the instrument, wherein the positioning of the one or more samples into a reading position is achieved using two phased recognition.

The two phased recognition preferably utilises at least two independent micro switches.

A first switch informs the instrument that the apparatus is within range and a second switches confirms precise alignment.

A first micro switch on the instrument is activated by an "element" on the apparatus and this constitutes the first phase of detection. Preferably the element on the apparatus is a projecting member which depresses a board mounted micro-switch via a rocker arm assembly. The rocker arm actuation overcomes any error in the horizontal location of the switch on the circuit board.

A second switch on the instrument serves as the "fine tune" and is activated when the instrument reaches a precise (as opposed to general) location on the instrument.

In one embodiment the two members of the switch are a notch in the outermost wall of the apparatus, more particularly a carousel or cassette type apparatus, and a resilient member or arm on the instrument. When the carousel or cassette type apparatus moves into position the resilient member or arm moves from a position in which the member is biased to its unbiased position thereby deactivating the switch.

This two stage recognition makes assembly easier and increases the robustness of operation. It also improves the ease of use.

In the case of a carousel device of the type disclosed in PCT/GB98/03586, it is preferred that there are a plurality of such switches.

More preferably there are four such switches located 90° apart.

A separate and unrelated problem with a device of the general type described in PCT/GB98/03586 is how to achieve good readings when quantifying two different fractions.

For example in the case of diabetes management it is desirable to determine the percentage of blood haemoglobin (Hb) that is glaciated. This means two assay results need to be obtained and a comparison made between them. For example between glaciated and non glaciated haemoglobin.

Traditionally analyses are measured at a peak frequency. In the case of glaciated proteins containing haem pigment this peak frequency is around 405nm. The applicant has determined that there are significant advantages

to be gained by making the measurements off peak, and in the case of glaciated haemoglobin protein, at between 415-460nm, more particularly still at about 440nm. This frequency range corresponds to be shoulder of the absorbance verses wavelength graph for haemoglobin. The 440 nm figure is the preferred wavelength. This extends the linear response to cover a wider and hence more useful range of haemoglobin concentrations.

According to this independent aspect of the present invention there is provided a method for determining the % glycation of blood comprising separating a blood sample into a first component fraction containing one or more non glaciated proteins, and a second component containing the one or more glaciated proteins, and detecting/quantifying the analyte by spectrophotometric means at between 405 nm and 460 nm, more preferably at about 440nm.

The "off peak" measurement avoids complicated calibration procedures, both in production and on-going in the field. It is essential for the performance of an instrument and when comparing tests between instruments that there is a linear response between measurement and concentration of absorbing substance. It is equally important that the range of linear response is wide enough so that measurement of, for example, both glaciated and unglycated fractions can be made on a linear portion of a response curve. The reason for this is that the slope of the linear response will vary for a number of reasons from instrument to instrument. Also the

slope of the linear response will also vary within an instrument as a function of temperature or other environmental factors. However, the nature of the calculation of % glycation is such that, within a given instrument, the slope of the response cancels out. Variations in slope do not therefore effect the result either within an instrument or between instruments, as long as significant change does not occur over the period of an assay. Any remaining variation between instruments can therefore be equalised using a calibrated offset established during initial set up at manufacture.

The use of a narrow band of wavelength produces a linear response but as this nears the absorbance maximum of haemoglobin the range of response is reduced. This is because at this point the system is at its maximum sensitivity. The selection of suitable band pass filters away from the absorbance maximum de-sensitises the system and extends the working range of the response allowing the elimination of slope factors described above. The reduced sensitivity is then offset by achieving a high signal to noise ratio on the detector electronics.

A separate and unrelated problem with a device of the general type described in PCT/GB98/03586 is ensuring accuracy of readings and keeping critical values (CV's) to a minimum.

The applicant has demonstrated that a major factor effecting critical values is ensuring all of the sample is collected for measuring. Thus where small volumes are measured as much as 8% of the total volume can be lost

in a single drop.

According to this independent aspect of the present invention there is provided an apparatus incorporating one or a plurality of means for breaking the surface tension of a drop to ensure it leaves a first component part and enters a second component part of an apparatus.

In one embodiment the means comprise a web or like member situated between the first and second components parts.

More preferably the apparatus is of a type in which an inlet port is movable relative to each of first and second inlets, said inlet port being funnel shaped and accommodating a filter means or binder retaining means, said web being situated across the outlet of said funnel.

A separate and unrelated problem with a device of the general type described in PCT/GB98/03586 is the problem of ensuring the apparatus is firmly held in position in the apparatus when readings are to be taken.

The Applicant has resolved this problem by careful design of the apparatus and instrument.

Thus in one embodiment the carousel apparatus comprises a tapered circumferential ring and the instrument comprises spring clips which pull the carousel downwards preventing wobble.

According to this independent aspect of the present invention there is provided a device comprising an instrument for reading one or more samples and an apparatus for presenting the one or more sample to the instrument,

wherein the apparatus is held firmly in position in the instrument by means of spring clips.

The main invention and various independent aspects of the invention will now be described, by way of example only with reference to a device of the general type described in PCT/GB98/03586 and a method of assaying glaciated and non glaciated haemoglobin fractions.

FIG. 1 is a perspective view of an apparatus according to one aspect of the invention;

FIG. 2 is a partial sectional view of the Fig. 1 apparatus;

FIG. 3 is a perspective view of the base portion of the apparatus of FIG. 2 showing the paddle of the invention; and

FIG. 4 is a perspective view of an instrument for use with an apparatus as illustrated in FIGS 1 to 3.

Referring to Figs. 1 and 2 the carousel apparatus 31 comprises a base section 2 of clear plastics (shown in detail in Fig. 3), a top portion 6 and a funnel portion 32. The funnel portion 32 is made of a hydrophobic plastics and has a relatively large aperture to simplify emptying of reagents therein. It has an outlet 34 which directs the liquid into the optical chambers 3 and 5 when the apparatus is rotated in an instrument. The outlet 34 includes a frit (not shown) which frit serves to retain particles such as, for example, an amino phenyl boronate agarose affinity matrix. The funnel 32 which serves as an inlet port has an annular rim 36 with a recessed portion 38. The rim

36 partially overlies apertures 40, 42 and 44 formed in the top portion 6 of the apparatus such that tubes vertically disposed in the apparatus cannot pass through the respective apertures until the apertures are aligned with the recessed portion 38 of the annular rim. Projecting from the underside of the funnel is a stem 48 with a female mating member via which the apparatus 31 is connected to the instrument 24 which has a male member 50 adapted to engage it. The male member 50 holds the funnel in a fixed position relative to the instrument 24 such that the base portion 2 and top portion 6 of the apparatus 31 which together form a carousel rotate around the funnel, the annular rim 36 of the funnel serving as a guide means.

The base portion 6 of the apparatus is made of a clear plastics, is generally annular in shape and is divided into a plurality of compartments. As can be seen from Fig. 3 there are two optical chambers 3 and 5, a third chamber 4, for receiving waste from a wash step, which third chamber is disposed between optical chambers 3 and 5, and three additional chambers 40', 42' and 44' each housing a reagent tube. These chambers 40', 42' and 44', which are disposed below apertures 40, 42 and 44 in the top portion 6 of the apparatus 31, are arranged so that the reagent tubes are presented to the user when the carousel is in the appropriate position in use. The optical chambers have a curved outer wall 52 and a curved inner wall 54 of optical quality, which help focus light from the LED's of the instrument 24 through the sample in the chamber to photodiodes at the other side thereof.

Each optical chamber 3, 5 can be brought into liquid communication with the outlet 34 of the funnel inlet port 9. Alternatively, the optical chambers can be recessed. Extending outwardly from the outermost wall 56 of the base portion 2 is a guide member 58 which sits within a circumferential channel member 60 formed on the outermost wall 62 of the annular recess 64 of the instrument 24. A communicating channel 66 which extends from the channel member 60 in outermost wall 62 to the top face 68 of the instrument 24 allows the guide member 58 to be inserted into the channel member 60 when the apparatus 31 is connected to the instrument 24.

A projecting member or tab 70 on the knurled edge 72 of the top portion 6 acts as an indicator means, denoting the position for locating the apparatus on the instrument and serves to assist in the turning of the apparatus.

The base portion 2 is connected to the top portion and the funnel portion sits in a channel 76 formed by a step on the top surface 78 of the top portion 6.

The instrument illustrated in Fig. 4 has been designed for use with a basic apparatus as herein before described. The instrument is provided with a power management and monitoring circuit so that the instrument can be connected to, for example, an external dc supply or a car battery. Additionally, the instrument is provided with a communication system such as, for example, a RS232 thereby providing means for sending and receiving

instructions and down loading data.

Significantly, the means for receiving the apparatus is an annular recess 64 in the instrument which is defined by a floor, an outermost sidewall 62 and an innermost sidewall 80.

The floor of the annular recess comprises a ramp 82 on a part thereof.

Within the outermost sidewall 62 of the annular recess is a channel member

60 and extending therefrom to the top surface a connecting channel 66.

In use the basic apparatus is inserted into the annular recess 60 by aligning guide member 58 of the apparatus with connecting channel 66 so that the apparatus is connected to male mating member 50 via its female mating member 48. The guide member 58 can thus enter channel member 60 such that it can be rotated. On rotation a first tube is directed up the ramp 82 and out of its aperture 44 since the recessed portion 38 of the annular ring 36 is aligned with the aperture. In this position the outlet 34 is in liquid communication with the first optical chamber 3 and the first step of the assay can be conducted. By turning the apparatus through a further 90° a wash solution is presented through aperture 42 for use and then on turning the apparatus though a further 90° tube 40, the eluting solution, is presented. In this manner the appropriate reagents are presented for each step of the assay process.

Having briefly described the favoured basic apparatus and instrument there follows a more detailed look at the improvements.

When tested an apparatus as described in PCT/GB98/03586 showed a critical value in the order of 6-7%. This was found to result primarily from an elution gradient forming when the glaciated fraction was eluted off the solid phase. In fact, it was found that the glaciated fraction was eluted off in a decreasing concentration as the elution buffer percolated into the optical chamber 5. Tests indicated that the first concentrated drops emerging from the funnel 32 collected in the corners of the optical chamber 5 and did not mix sufficiently with the more dilute drips that followed. As a result measurements taken before mechanical mixing of the solution showed poorer precision and an "off set" from those recorded post mixing.

To overcome this problem it proved necessary to introduce a mixing step.

However traditional methods proved unsuitable. Thus, for example, the apparatus could not be shaken without fear of damage to the instrument, and the use of a rotating flea or oscillating ball bearing could damage the optical chamber.

The applicant solved the problem using a paddle 100. A number of approaches were used:

Retention of a stirring device was seen as the major issue to be resolved. Attaching a stirring component to the side walls of the optical chamber was seen as a possible approach to overcome this problem. Two alternatives were investigated: In one embodiment the paddle was

clipped over the side walls of the optical chamber and the paddle was made to vibrate in the direction of the optical axis using an electromagnet. A hole in the centre of the paddle provides a path for the light from the LED.

In another embodiment the paddle was clipped over one side of the optical chamber 5 and was made to vibrate at right angles to the optical axis away from the light path.

Both these embodiments provided adequate mixing once a resonant frequency was found by adjusting the frequency of an oscillator driving an electromagnet. Though attractive there were still a number of problems with this approach.

As the paddle must retain stiffness a significant amount of energy was required to generate the oscillation. This would have implications for any battery operated instrument.

Furthermore resonant frequencies vary from component to component and with the liquid level within a chamber. Some means of scanning the frequencies would thus be required to hit resonance and thus ensure adequate mixing. Since both components also had a 3-dimensional shape forming was required increasing costs.

An alternative approach of using a flat paddle overcame the problems associated with the oscillating approach described above.

Thus in a preferred embodiment and as illustrated in Fig.3 a metal paddle 100 was retained in grooves 101 formed by building-up the side walls

102, 104 of the optical chamber 5. The paddle was able to reciprocate with minimal friction and could be forced to swing through the solution, along the direction of the optical axis, using an electromagnet positioned below the photodiode on the outer circumference of the platten moulding (described hereafter). A hole 106 is provided to enable the light from the LED to reach the detector.

As very little force is necessary to move the paddle, significantly less energy is required to drive the electromagnet. Experiments have shown that fewer than 10 swings of the paddle are required to produce a visually homogenous solution from a layered dye-water starting solution.

Effective retention of the paddle has been demonstrated by positioning a web (not shown) on the underside of the top moulding 6, just above the centre of the paddle.

Another improvement relates to the use of 2 micro-switches in a phased approach. This allows the precise unambiguous detection of the apparatus 31 in the instrument 24. One switch (not shown) at each of four locations is activated by a feature 58 (in this case also the guide member) on the circumference of the plastic well as it rotates. This depresses a board mounted micro-switch (not shown) via a rocker arm assembly (110, 112, 114 & 116) at each of the four operating positions (Fig. 4). The rocker arm actuation overcomes any error in the horizontal location of the switch on the circuit board (not shown). This constitutes the first phase of detection.

The second phase of detection is provided by a micro-switch which is activated by the operation of a ratchet arm not shown with a respective notch or notches 120, 122, (only two of the four are visible) in the outermost wall 56 of the carousel. A flange 131 extending from the ratchet arm contacts a switch on the instrument. The ratchet arm is biased such that when the carousel is in one of the four operating positions it moves into a notch in the carousel, deactivating the switch but when it is not in one of these positions it is acted against by the outermost wall 56 of the carousel causing the switch to be activated. These notches are preferably shaped to allow rotation in one direction only. These switches are only de-activated when the instrument and apparatus are in an exact location. The two phased approach makes assembly easier, increases robustness of operation and improves ease of use.

Finally another improvement relates to the arrangement used to overcome a 'wobble' problem. Any movement, however small, between the carousel and instrument can alter the path of light during reading. By modifying the carousel and instrument to provide a lock facility the reading problem was overcome.

In one embodiment the carousel comprises (Fig.1) a circumferential ring 124 comprising an inclined surface 126 and a flat surface 128.

The instrument 24 which receives the carousel comprises a casing 130, a printed circuit board 132 onto which is mounted a plateen 134 and a

hold down 136 comprising four spring clips 138, 140, 142, 144. When the carousel is inserted into the instrument, the spring clips ride up the inclined surface 126 and their claws lock against the flat surface 128.

#### **CLAIMS**

- 1. A method of mixing a sample in a chamber (3, 5) comprising positioning a paddle (100) in the sample and causing said paddle to undergo a reciprocating motion.
- 2. A method a claimed in claim 1 wherein the paddle is of a magnetic material and comprises a liquid moving surface and means for supporting the paddle in or over the chamber and said paddle is caused to undergo a reciprocating motion by the action of an electromagnetic means.
- 3. A method as claimed in claim 2 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface which arms sit in a pair of slots in sides extending from a base which defines the chamber.
- 4. A method as claimed in either claim 2 or 3 which further comprises detecting an analyte in said sample by passing a light beam from a light emitter through said chamber and an opening (106) formed in the liquid moving surface of said paddle to a light detector.
- 5. A method as claimed in claim 4 wherein the sample is glycated haemoglobin and is detected by a spectrophotometric means at between 405 nm and 460 nm.
- 6. A paddle (100) comprising a liquid moving surface and means for supporting said paddle in or over a chamber such that the paddle can undergo a reciprocating motion in the chamber.

- 7. A paddle as claimed in claim 6 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface.
- 8. A paddle as claimed in either claim 6 or 7 wherein the paddle is T shaped.
- 9. A paddle as claimed in any of claim 6,7 or 8 wherein the liquid moving surface has an opening (106) formed therein through which a light beam can pass.
- 10. A paddle as claimed in any of claims 6 to 9 wherein the paddle comprises a magnetic material.
- 11. A paddle as claimed in any of claims 6 to 9 wherein the paddle comprises a piezoelectric material.
- 12. A sample container comprising a chamber (3, 5) adapted to receive a paddle (100), said paddle being mounted in or over said chamber such that the paddle can undergo a reciprocating motion in the chamber.
- 13. A sample container as claimed in claim 12 comprising a base with sides extending therefrom to define the chamber, said sides comprising means which support the paddle.
- 14. A sample container as claimed in claim 13 wherein said means which support the paddle is a pair of slots in said sides.
- 15. A sample container as claimed in any of claims 12-14 in which said chamber is an optical chamber.

- 16. A sample container as claimed in any of claims 12-15 which is a carousel or cassette.
- 17. A carousel as claimed in claim 16, for use in an assay in which a sample is separated into a first component fraction and a second component fraction, which fractions are presented to an instrument, comprising a first inlet which is or leads to a first component fraction collection chamber, a second inlet which is or leads to a second component fraction collection chamber, and an inlet port accommodating a filter means or a binder retaining means, said inlet port being movable relative to each of said first and second inlets such that the inlet port can be brought into liquid communication with each first and second inlet in turn as required.
- 18. A sample container as claimed in claim 16 which is a carousel comprising a base portion having a plurality of chambers including first and second inlets, a top portion which together with the base portion forms the carousel, and a funnel portion including an inlet port, said carousel being rotatably mounted about said funnel portion.
- 19. An instrument adapted to receive a sample container comprising a chamber adapted to receive a paddle, said instrument comprising means for causing said paddle to undergo a reciprocating motion in the chamber.
- 20. An apparatus as claimed in claim 19 in which said means for causing said paddle to undergo a reciprocating motion is an electromagnetic means.

- 21. An apparatus as claimed in claim 20 wherein said electromagnetic means is a solenoid.
- 22. A device comprising an instrument capable of detecting an analyte in a sample which is presented thereto in a sample container comprising a chamber adapted to receive a paddle said paddle being mounted in or over said chamber such that said paddle can undergo a reciprocating motion when initiated by said instrument.
- 23. A device, comprising an instrument for reading one or more samples, and an apparatus for presenting the one or more samples to the instrument, wherein the positioning of the one or more samples into a reading position is achieved using two phased recognition.
- 24. A device as claimed in claim 23 in which a first switch informs the instrument that the apparatus is within range and a second switches confirms precise alignment.
- 25. A device as claimed in claim 23 or 24 wherein a first micro switch on the instrument is activated by an "element" on the apparatus and this constitutes the first phase of detection and a second switch on the instrument serves as the "fine tune" and is activated when the instrument reaches a precise location on the instrument.
- 26. A device as claimed in claim 25 wherein the "element" on the apparatus is a projecting member which depresses a board mounted microswitch via a rocker arm assembly.

- 27. A device as claimed in claim 26 wherein the two members of the switch are a notch in the outermost wall of the apparatus, and a resilient member or arm on the instrument.
- 28. A device as claimed in claim 27 wherein the apparatus is a carousel or cassette type apparatus.
- 29. A device as claimed in claim 28 comprising four switches located 90° apart.
- 30. A method for determining the percentage glycation of blood comprising separating a blood sample into a first component fraction containing one or more non glycated proteins, and a second component containing the one or more glycated proteins, and detecting/quantifying glycated haemoglobin by spectrophotometric means at between 405 nm and 460 nm.
- 31. A method as claimed in claim 30 wherein the detection/quantification of glycated haemoglobin is measured at about 440nm.
- 32. An apparatus incorporating one or a plurality of means for breaking the surface tension of a drop to ensure it leaves a first component part and enters a second component part of an apparatus.
- 33. An apparatus as claimed in claim 32 in which the means comprise a web or like member situated between the first and second component parts.

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- 34. An apparatus as claimed in claim 32 or 33 wherein the apparatus is of a type in which an inlet port is movable relative to each of first and second inlets which are or lead to first and second collection chambers, said inlet port being a funnel and accommodating a filter means or binder retaining means, said web being situated across an outlet of said funnel.
- 35. A device comprising an instrument for reading one or more samples and an apparatus for presenting the one or more sample to the instrument, wherein the apparatus is held firmly in position in the instrument by means of spring clips.

#### (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

## (19) World Intellectual Property Organization International Bureau



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### (43) International Publication Date 21 December 2000 (21.12.2000)

#### **PCT**

## (10) International Publication Number WO 00/76642 A2

(51) International Patent Classification7:

(21) International Application Number: PCT/GB00/02259

(22) International Filing Date: 9 June 2000 (09.06.2000)

(25) Filing Language:

English

B01F

(26) Publication Language:

English

(30) Priority Data: 9913560.0

10 June 1999 (10.06.1999) GF

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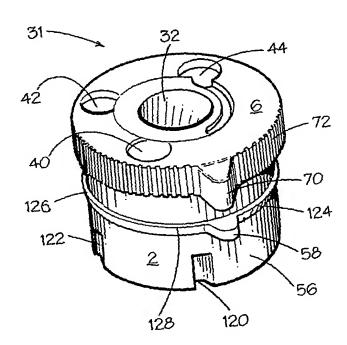
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[Continued on next page]

(54) Title: MIXING APPARATUS AND METHOD OF MIXING



(57) Abstract: Apparatus, instrument, device and a method of mixing for conducting an assay. Apparatus comprising a first and second inlet and an inlet port accommodating a filter and/or binder retaining means, the inlet port moveable relative to first and second inlets such that the port can be brought into liquid communication with each inlet, and a sample chamber comprising a paddle wich undergeos a reciprocating motion.



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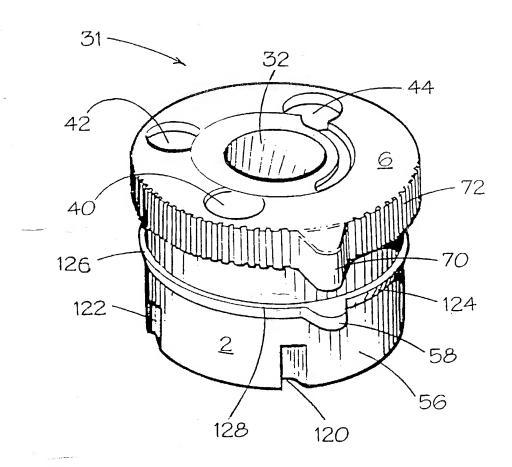


FIG. 1.

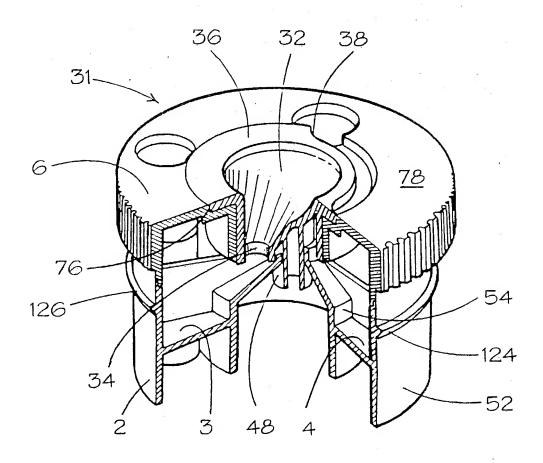


FIG. 2.

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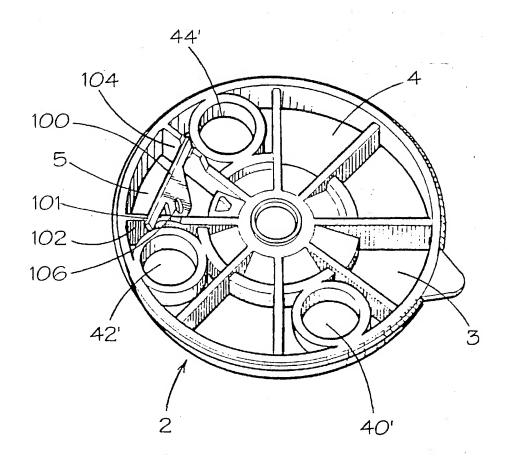
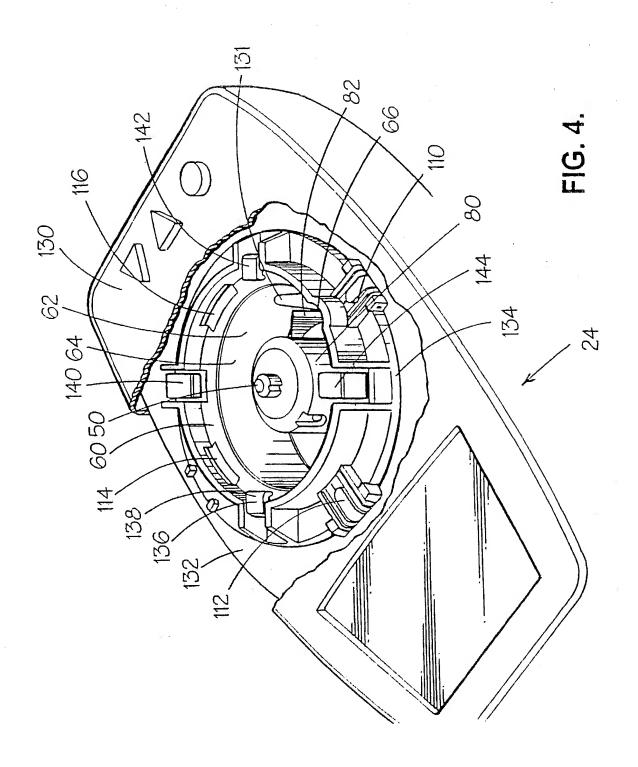


FIG. 3.

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David ANDREWES, et al.

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## ADDITIONAL INVENTOR(S) Supplemental Sheet Page 1 of 4

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ADDITIONAL INVENTOR(S)
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Felix	×		•		F	ERI	NANDO				
Inventor's Signature									Date		
Residence: City	Wokingham	State	Berks (GI	3)	Count	ry	υĸ	Cit	izenship	UK	
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Residence: City	Broughton State Chester (GB) Country UK Citizenship UK							υĸ			
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Inventor's Signature										Date	
Residence: City	Balderton	Sta	ıte	Chester (GB	) [	Country	y 	UK		Citizenship	UK
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David Ala	an	n PERCIVAL									
Inventor's Signature										Date	
Residence: City	Hawarden	Sta	tate	Flintshire (	(GB)	Со	untry	y UI	κ	Citizenship	UK
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<b>∂</b> John Ant	thony O'DELL C							C.			
Inventor's Signature		Date									
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## **DECLARATION** – Utility or Design Patent Application

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☐ Additional registered practitioner(s) named on supplemental sheet PTO/SB/02C attached hereto.  Direct all correspondence to: ☐ Customer Number 25235 OR ☐ Correspondence or Bar Code Label PATENT TRADEMARK OFFICE address below												
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## ADDITIONAL INVENTOR(S) Supplemental Sheet Page 1 of 4

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Felix					FE	RNA	NDO			
Inventor's Signature								Date		
Residence: City	Wokingham	State	Berks (G	В)	Country	U	K Ci	tizenship	UK	
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Residence: City	Chester	State	Chester	(GB)	Count	ry	uk -	Citizenship	UK	. /
Post Office Address	4 Beaumont	Close	GB							
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Residence: City	Broughton	State	Chester	(GB)	Coun	try	υĸ	Citizens	hip	υκ
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David Ala	an	PERCIVAL										
Inventor's Signature			-								Date	
Residence: City	Hawarden	\$	State	Flintshire	(GE	3)	Coun	itry	ט	κ	Citizenship	UK
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<sub>7</sub> John Ant	thony O'DELL								. (			
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Residence: City	Balderton	St	ate	London (G	B)	Co	ountry		υĸ	C	Citizenship	UK
Post Office Address	24 Halford Road											
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# ADDITIONAL INVENTOR(S) Supplemental Sheet Page 4 of 4

Name of Additional Joi any:	nt Inventor, if	☐ A petition has been filed for this unsigned inventor											
Given Name (first and	d middle [if any])		. Fa	amily Na	ame c	or Surname	e						
Adrian Ri	chard		GRAY										
Inventor's Signature								Date					
Residence: City	Vaughans Lane	State	Chester (GB)	Coun	try	υĸ	Citizenship						
Post Office Address	West End Ho	ouse											
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City	Vaughans Lane	State	Chester (BG)	Z	ΊΡ	СН3 5	5XF Country UK						
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Inventor's Signature								Date	,				
Residence: City		State		Cou	untry		Cit	izenship					
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**COMPLETE IF KNOWN** 

**WPT0006** 

David ANDREWES, et al.

(37 CFR	(1.03)	Application Number	10/009,27	7								
☐ Declaration OR ☐ Submitted	☑ Declaration to be Submitted after	Filing Date	D	ecember 7,	2001							
with Initial	Initial Filing	Group Art Unit										
Filing	surcharge 37 CFR 1.16(e) required	Examiner Name										
As a below named Inventor	r, I hereby declare that:											
My residence, post office address, and citizenship are as stated below next to my name.												
I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:												
MIXING APPARATUS AND METHOD OF MIXING DURING												
CONDUCTING AN ASSAY												
		No										
the specification of which												
is attached hereto												
OR												
was filed on (MM/DD/YYYY)	12/07/2001	as U.S. Application N PCT International App										
and was amended on (MM/DD/YYYY)		(if applicable)										
I hereby state that I have re claims, as amended by any			dentified spe	cification, inclu	ding the							
I hereby claim foreign prior inventor's certificate, or § 3 the United States of Americ for patent or inventor's cert application on which priorit	65(a) of any PCT interna ca, listed below and have ificate, or of any PCT inte	ational application which de a also identified below, by c	signated at le hecking the l	east one countr box, any foreigr	y other than application							
Prior Foreign Appl. No.(s)	Country	Foreign Filing Date F (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Yes	Attached? No							
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I hereby claim the benefit u			sional applica	ation(s) listed be	elow.							
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Attorney Docket No.

**First Named Inventor** 

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**DECLARATION FOR** 

**UTILITY OR DESIGN** 

PATENT APPLICATION

### **DECLARATION** – Utility or Design Patent Application

application d claims of this provided by patentability	I hereby claim the benefit under 35 U.S.C. 120 of any U.S. application(s) or 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application												
		plication or				arent Fili (MM/DE			P	arent F (if app			
☐ Addition	Additional U.S. or PCT international application nos. listed on PTO/SB/02B attached hereto.												
As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent Trademark Office connected therewith:  Customer Number  OR  Registered practitioner(s) name/registration number listed below													
Registration Registration Name Number Name Number													
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Additional registered practitioner(s) named on supplemental sheet PTO/SB/02C attached hereto.													
☐ Additional registered practitioner(s) named on supplemental sheet PTO/SB/02C attached hereto.  Direct all correspondence to: ☐ Customer Number 25235 OR ☐ Correspondence  or Bar Code Label PATENT TRADEMARK OFFICE address below													
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[Page 2 of 2]

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## ADDITIONAL INVENTOR(S) Supplemental Sheet Page 1 of 4

Name of Additional Jo	oint Inventor, if any	·:		☐ A petition has been filed for this unsigned inventor								
Given Name (firs	and middle [if any]	)			F	amily N	lame or	Surnam	e			
John W	orthington			ATTRIDGE								
Inventor's Signature									Date			
Residence: City	Ripley	State	Surrey (GB)   Country   UK   Citizenship   UI							UK		
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Anthor	ny				ST	EVE	NSON			
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Residence: City	Chester	State	Chester (	GB)	Coun	try	υK	Citizenship	UI	Κ
Post Office Address	4 Beaumont	Close								
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	Inventor's Signature	4	H	1			7			Date	28/3/02	
	Residence: City	Balderton	Sta	te	Chester (GB	) (	Country	UK	(	Citizenship	UK	
	Post Office Address	Balderton I	lous	se	GBX	 ;			<b>-</b>			
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O	Inventor's Signature	$\subseteq$	)	V						Date	28/3/02	
	Residence: City	Hawarden	Sta	ate	Flintshire	(GB)	Coun	try U	K	Citizenship	UK	
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	John Ant	hony					0	'DELL				
	Inventor's Signature									Date		
	Residence: City	Balderton	Stat	te	London (GB	) (	Country	ик		Citizenship	UK	
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#### **DECLARATION**

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ADDITIONAL INVENTOR(S)
Supplemental Sheet
Page \_\_4\_\_ of \_\_4\_\_

Name of Additional Joi any:	al Joint Inventor, if						or						
Given Name (first and	d middle [if any])			Family	Name o	or Surname	•						
Adrian Ri	chard		GRAY										
Inventor's Signature								Date					
Residence: City	Vaughans Lane	State	Chester (GB)	Cou	intry	υκ	Citizenship UK						
Post Office Address	West End Ho	puse											
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WPT0006

David ANDREWES, et al.

(37 CFR	ł 1.63)	Application Number	10/009,27	77								
	Declaration to be	Filing Date	D	ecember 7,								
Submitted with Initial	Submitted after Initial Filing	Group Art Unit										
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<u>-</u>	1.10(e) required	Examiner Name										
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My residence, post office address, and citizenship are as stated below next to my name.												
I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:												
MIXING APPARATUS AND METHOD OF MIXING DURING												
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the specification of which												
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I hereby state that I have re			dentified spe	ecification, inclu	uding the							
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I hereby claim foreign prior inventor's certificate, or § 3 the United States of Amerifor patent or inventor's cert application on which priorit	65(a) of any PCT interna ca, listed below and have ificate, or of any PCT into	ational application which de also identified below, by c	signated at le hecking the	east one count box, any foreig	try other than In application							
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Attorney Docket No.

First Named Inventor

**DECLARATION FOR** 

**UTILITY OR DESIGN** 

PATENT APPLICATION

## ADDITIONAL INVENTOR(S) Supplemental Sheet Page 4 of 4

Name of Additional Jo any:	Int Inventor, if		ப A pelition has been filed for this unsigned inventor										
Given Name (first and	d middle [if any])	-14-		=amily N	Jame	or Suman	10						
Adrian Ri	chard		GRAY										
inventor'e Signature								Date					
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John	<del></del> , .					CUI	RTIS			
Inventor's Signature									Date	
Residence: City	Baiderton	State	ete Chester (GR) Country UK Citizenship L							UK
Post Office Address	Balderton H	ouse	se .							
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Name of Additional Jo any:	Int Inventor, If		ΠA	pelition	has bee	n file	ed for this	unsiç	ined inventor	
Given Name (first and r	middle [if any])	Family Name or Surname								
David Ala	an	PERCIVAL						i		
Inventor's Signature									Date	
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COMPLETE IF KNOWN

WPT0006

David ANDREWES, et al.

(37 CFF	(1.63)	Application Number		10/009,277								
☐ Declaration OR Submitted	Declaration to be Submitted after	Filing Date	Dec	cember 7, 2001								
with Initial	Initial Filing	Group Art Unit		•								
Filing	surcharge 37 CFR 1.16(e) required	Examiner Name										
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As a below named Invento	or, I hereby declare that:	,										
My residence, post office address, and citizenship are as stated below next to my name.												
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Prior Foreign Appl. No.(s	) Country		rity Not C aimed	ertified Copy Attached? Yes No								
PCT/GB00/02259	WIPO	06/09/2000										
9913560.0	GB	06/10/1999										
Additional foreign application nos. are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:												
		of any United States provision	nal application	on(s) listed below.								
Application Number(s)	Filing Date (MM/DD/Y	YYY)										

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## ADDITIONAL INVENTOR(S) Supplemental Sheet Page 4 of 4

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